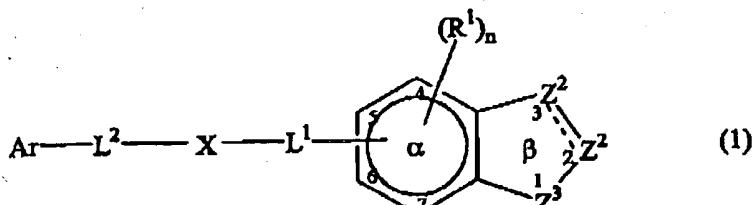


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CLAIM AMENDMENTS

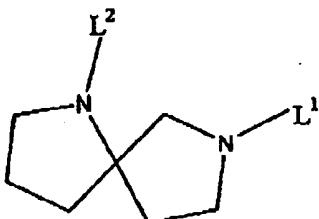
1. (currently amended) A compound of the formula:



*[Handwritten note: 1/2 entered 10/4/04]*  
and the pharmaceutically acceptable salts thereof wherein:

Ar is an aryl group substituted with 0-5 non-interfering substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aryl, halo, OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, R<sub>3</sub>Si, and NO<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members;

L<sup>2</sup>-X-L<sup>1</sup> is of the formula:



L<sup>1</sup> is CO, SO<sub>2</sub> or alkylene (1-4C);

L<sup>2</sup> is alkylene (1-4C) or alkenylene (2-4C) optionally substituted with one or two moieties selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, NH-aryl, halo, OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOCR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, and R<sub>3</sub>Si, wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N atoms, and wherein two substituents on L<sup>2</sup> can be joined to form a non-aromatic saturated or unsaturated

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ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety;

n is 0-3;

each R<sup>1</sup> is independently halo, alkyl, heteroalkyl, OCOR, OR, NRCOR, SR, or NR2, wherein R is hydrogen, alkyl, or aryl, or forms thereof containing 1-2 O, S and/or N;

 represents a single or double bond;

one Z<sup>2</sup> is CA or CR<sup>2</sup>A; the other Z<sup>2</sup> is CR<sup>3</sup>, CR<sup>3</sup><sub>2</sub>, NR<sup>4</sup> or N; and each R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-arylo, halo, OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, R<sub>3</sub>Si, and NO<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N and two of R<sup>2</sup> and/or R<sup>3</sup> on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R<sup>2</sup> and/or R<sup>3</sup> is =O or an oxime, oximeether, oximeester or ketal thereof;

Z<sup>3</sup> is NR<sup>5</sup> or O; where R<sup>5</sup> is H or is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO<sub>2</sub>R, RCO, COOR, alkyl-COR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, NR<sub>2</sub>, OR, alkyl-SR, alkyl-SOR, alkyl-SO<sub>2</sub>R, alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl-CONR<sub>2</sub>, or R<sub>3</sub>Si, wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N;

A is -W<sub>i</sub>-COX<sub>j</sub>Y, where Y is COR<sup>6</sup> or an isostere thereof, selected from tetrazole, 1,2,3-triazole, 1,2,4-triazole and imidazole, each of W and X is substituted or unsubstituted alkylene or alkenylene, each of 2-6Å; each of i and j is independently 0 or 1; and R<sup>6</sup> is H, or is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, SOR, SO<sub>2</sub>R, SO<sub>2</sub>NR<sub>2</sub>, OR, NR<sub>2</sub>, OCOR, NRCOR, NRCONR<sub>2</sub>, NRSO<sub>2</sub>R, NRSO<sub>2</sub>NR<sub>2</sub>, OCONR<sub>2</sub>, CN, COOR, CONR<sub>2</sub>, COR, or R<sub>3</sub>Si wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N, or

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wherein R<sup>6</sup> is OR, NR<sub>2</sub>, SR, NRCNR<sub>2</sub>, OCONR<sub>2</sub>, or NRSO<sub>2</sub>NR<sub>1</sub>, wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof; and wherein two R attached to the same atom may form a 3-8 member carbocyclic or heterocyclic ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR<sub>2</sub>, OCOR, NRCOR, NRCNR<sub>2</sub>, NRSO<sub>2</sub>R, NRSO<sub>2</sub>NR<sub>2</sub>, OCONR<sub>2</sub>, or R<sub>3</sub>Si wherein each R is independently H, alkyl, alkenyl or aryl or forms containing 1-2 O, S and/or N wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined.

2. (canceled)

2 3. (original) The compound of claim 1 wherein Y is an isoster of COR<sup>6</sup>.

3 4. (original) The compound of claim 3 wherein Y is tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole.

4 5. (original) The compound of claim 1 wherein each of i and j is 0.

5 6. (previously presented) The compound of claim 1 wherein j is 0.

6 7. (original) The compound of claim 1 wherein Z<sup>3</sup> is NR<sup>5</sup>.

8. (canceled)

7 9. (previously presented) The compound of claim 1 wherein R<sup>5</sup> is H, or is optionally substituted alkyl or acyl.

10-11. (canceled)

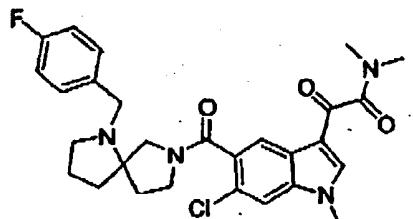
8 12. (previously presented) The compound of claim 1 wherein R<sup>2</sup> and R<sup>3</sup> are independently selected from halo, OR and alkyl.

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13-38. (canceled)

9 39. (previously presented) The compound of claim 1 wherein the compound is:

10 40. (currently amended) The compound of claim 1 wherein L<sup>1</sup> is CH<sub>2</sub> or CO and L<sup>2</sup> are independently selected from CO, CHOH, CH<sub>2</sub>-NH-CO, CH<sub>2</sub>-N-CH<sub>3</sub>, and is CH<sub>2</sub> or CHOH.11 41. (currently amended) The compound of claim 40 wherein L<sup>1</sup> and/or L<sup>2</sup> is CO.

42-44. (canceled)

12 45. (previously presented) The compound of claim 1 wherein L<sup>2</sup> and/or L<sup>1</sup> is unsubstituted alkylene.13 46. (previously presented) The compound of claim 1 wherein L<sup>2</sup> and/or L<sup>1</sup> is unsubstituted methylene, or methylene substituted with alkyl.

47. (canceled)

14 48. (previously presented) The compound of claim 1 wherein Ar is optionally substituted phenyl.

15 49. (original) The compound of claim 48 wherein said optional substitution is by halo, OR, or alkyl.

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16  
50. (original) The compound of claim 49 wherein said phenyl is unsubstituted or has a single substituent.

51. (canceled)

17 52. (previously presented) The compound of claim 1 wherein R<sup>1</sup> is halo or alkoxy.

18 53. (original) The compound of claim 52 wherein n is 0, 1 or 2.

19 54. (original) The compound of claim 1 wherein L<sup>1</sup> is coupled to the α ring at the 4-, 5- or 6-position.

20 55. (original) The compound of claim 1 wherein Z<sup>2</sup> at position 3 is CA or CHA.

21 56. (original) The compound of claim 55 wherein the Z<sup>2</sup> at position 2 is CR<sup>3</sup> or CR<sup>3</sup>.

22 57. (currently amended) The compound of claim 56 wherein R<sup>3</sup> is hydrogen, or is selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aryloyl, halo, OR, NR<sub>2</sub>, SR, SOR, SO<sub>2</sub>R, OCOR, NRCOR, NRCONR<sub>2</sub>, NRCOOR, OCONR<sub>2</sub>, RCO, COOR, alkyl-OOR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, NRSO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, R<sub>3</sub>Si, and NO<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N and two of R<sup>1</sup> can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

23 58. (currently amended) The compound of claim 57 wherein each R<sup>3</sup> is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR<sub>2</sub>, SR, NRCOR, alkyl-OOR, RCO, COOR, and CN, wherein each R is independently H, alkyl[;] or aryl or forms thereof containing 1-2 O, S and/or N.

24 59. (original) The compound of claim 55 wherein Z<sup>2</sup> at position 2 is N or NR<sup>4</sup>.

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25 60. (currently amended) The compound of claim 59 wherein R<sup>4</sup> is H, or alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO<sub>2</sub>R, RCO, COOR, alkyl-COR, SO<sub>3</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, or R<sub>3</sub>Si wherein each R is independently H, alkyl, alkenyl or aryl or forms thereof containing 1-2 O, S and/or N.

26 61. (currently amended) The compound of claim 1 wherein ~~—~~ represents a double bond.

62. (canceled)

27 63. (currently amended) A pharmaceutical composition for treating conditions characterized by enhanced p38 ~~α~~ activity which composition comprises a therapeutically ~~an~~ effective amount of a compound of claim 1 and a pharmaceutically acceptable excipient.

64-67. (canceled)

28 68. (currently amended) [The] A method to treat of claim 67 wherein said preinflammation response is multiple sclerosis, IBD, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, other arthritic conditions, sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, asthma, adult respiratory distress syndrome, stroke, reperfusion injury, CNS injury, psoriasis, restenosis, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcoidosis, a bone resorption disease, graft versus host reaction, Crohn's Disease, ulcerative colitis, Alzheimer's or pyrexia which comprises administering to a subject in need of such treatment a compound of claim 1 or a pharmaceutical composition thereof.